



KRAS gene

KRAS proto-oncogene, GTPase

Normal Function

The *KRAS* gene provides instructions for making a protein called K-Ras that is involved primarily in regulating cell division. As part of a signaling pathway known as the RAS/MAPK pathway, the protein relays signals from outside the cell to the cell's nucleus. These signals instruct the cell to grow and divide or to mature and take on specialized functions (differentiate). The K-Ras protein is a GTPase, which means it converts a molecule called GTP into another molecule called GDP. The K-Ras protein acts like a switch, and it is turned on and off by the GTP and GDP molecules. To transmit signals, the K-Ras protein must be turned on by attaching (binding) to a molecule of GTP. The K-Ras protein is turned off (inactivated) when it converts the GTP to GDP. When the protein is bound to GDP, it does not relay signals to the cell's nucleus.

The *KRAS* gene belongs to a class of genes known as oncogenes. When mutated, oncogenes have the potential to cause normal cells to become cancerous. The *KRAS* gene is in the Ras family of oncogenes, which also includes two other genes: *HRAS* and *NRAS*. These proteins play important roles in cell division, cell differentiation, and the self-destruction of cells (apoptosis).

Health Conditions Related to Genetic Changes

autoimmune lymphoproliferative syndrome

cardiofaciocutaneous syndrome

Mutations in the *KRAS* gene are an uncommon cause of cardiofaciocutaneous syndrome, accounting for less than 5 percent of cases. Several mutations in the *KRAS* gene have been identified in people with characteristic features of the disorder, which include heart defects, distinctive facial features, and skin abnormalities. The mutations change single protein building blocks (amino acids) in the K-Ras protein. The altered protein shows increased GTP binding and a decreased ability to convert GTP to GDP. These effects lead to prolonged activation of the K-Ras protein, which alters tightly regulated RAS/MAPK signaling during development. The altered signaling interferes with the development of organs and tissues throughout the body, leading to the varied signs and symptoms of cardiofaciocutaneous syndrome.

cholangiocarcinoma

core binding factor acute myeloid leukemia

epidermal nevus

lung cancer

At least three mutations in the *KRAS* gene have been associated with lung cancer, a disease in which certain cells in the lung become abnormal and multiply uncontrollably to form a tumor. These mutations are somatic, which means they are acquired during a person's lifetime and are present only in tumor cells. Somatic mutations are not inherited. Nearly all of the *KRAS* gene mutations associated with lung cancer change the amino acid glycine at position 12 or 13 (Gly12 or Gly13) or change the amino acid glutamine at position 61 (Gln61) in the K-Ras protein. These mutations lead to a K-Ras protein that is constantly turned on (constitutively activated) and directing cells to grow and divide in an uncontrolled way, leading to tumor formation. When these gene changes occur in cells in the lungs, lung cancer develops.

KRAS gene mutations are found in 15 to 25 percent of all lung cancer cases but are more frequent in affected white populations compared to affected Asian populations; 25 to 50 percent of whites with lung cancer have *KRAS* gene mutations, whereas 5 to 15 percent of Asians with lung cancer have *KRAS* gene mutations.

While genetic, environmental, and lifestyle factors, including long-term tobacco smoking, contribute to a person's cancer risk, *KRAS* gene mutations are much more common in nonsmokers with lung cancer than in smokers. Lung cancers with *KRAS* gene mutations typically indicate a poor prognosis and resistance to several cancer treatments.

Noonan syndrome

other cancers

Somatic mutations in the *KRAS* gene are involved in the development of several types of cancer, particularly pancreatic and colorectal cancers. These mutations lead to a K-Ras protein that is more strongly overactivated than the mutations that cause cardiofaciocutaneous syndrome (described above). The abnormal K-Ras protein is always active and can direct cells to grow and divide in an uncontrolled way.

other disorders

KRAS gene mutations also cause a disorder whose major features overlap with those of cardiofaciocutaneous syndrome and two related disorders called Noonan syndrome and Costello syndrome. This condition has been described as the *KRAS* mutation-associated phenotype. People with this condition have variable signs and symptoms that include mild to moderate intellectual disability, distinctive facial

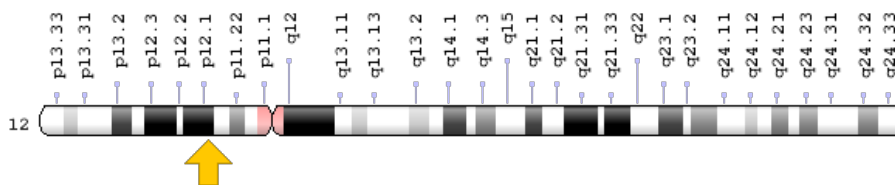
features, short stature, an unusually large head (macrocephaly), and hair that is sparse and thin.

At least nine mutations in the *KRAS* gene have been reported in people with this disorder. These mutations are present in all of the body's cells and are known as germline mutations. Each of these mutations changes single amino acids in the K-Ras protein. These genetic changes abnormally activate the protein, which alters chemical signaling in cells throughout the body. The altered signaling interferes with the normal development of many organs and tissues, resulting in the characteristic features of the *KRAS* mutation-associated phenotype.

Chromosomal Location

Cytogenetic Location: 12p12.1, which is the short (p) arm of chromosome 12 at position 12.1

Molecular Location: base pairs 25,204,789 to 25,252,093 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C-K-RAS
- c-K-ras protein
- c-K-ras2 protein
- c-Kirsten-ras protein
- cellular c-Ki-ras2 proto-oncogene
- K-ras p21 protein
- KI-RAS
- Kirsten rat sarcoma viral oncogene homolog
- KRAS1
- PR310 c-K-ras oncogene

- RASK2
- RASK_HUMAN
- transforming protein p21
- v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog

Additional Information & Resources

Educational Resources

- Genomes (second edition, 2002): Signal Transduction with Many Steps Between Receptor and Genome
<https://www.ncbi.nlm.nih.gov/books/NBK21127/#A7903>
- Immunobiology: The Immune System in Health and Disease (fifth edition, 2001): Small G Proteins Activate a Protein Kinase Cascade That Transmits the Signal to the Nucleus
<https://www.ncbi.nlm.nih.gov/books/NBK27151/#A684>
- Molecular Biology of the Cell (fourth edition, 2002): MAP Kinase Pathways
<https://www.ncbi.nlm.nih.gov/books/NBK21529/>
- Molecular Biology of the Cell (fourth edition, 2002): Ras Is Activated by a Guanine Nucleotide Exchange Factor
<https://www.ncbi.nlm.nih.gov/books/NBK26822/#A2855>

GeneReviews

- Cardiofaciocutaneous Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1186>
- Costello Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1507>
- Noonan Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1124>

Genetic Testing Registry

- GTR: Genetic tests for KRAS
<https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3845%5Bgeneid%5D>

Scientific articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28KRAS%5BTI%5D%29+OR+%28c-K-ras+protein%5BMAJR%5D%29%29+AND+%28genes%5BMH%5D%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D>

OMIM

- COLORECTAL CANCER
<http://omim.org/entry/114500>
- PANCREATIC CANCER
<http://omim.org/entry/260350>
- V-KI-RAS2 KIRSTEN RAT SARCOMA VIRAL ONCOGENE HOMOLOG
<http://omim.org/entry/190070>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/KRASID91.html>
- Cancer Genetics Web
<http://www.cancerindex.org/geneweb/KRAS2.htm>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=KRAS%5Bgene%5D>
- HGNC Gene Family: RAS type GTPase family
<http://www.genenames.org/cgi-bin/genefamilies/set/389>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6407
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/3845>
- UniProt
<http://www.uniprot.org/uniprot/P01116>

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